

In re application of : Barbera-Guillem, et al.

Application No. : 10/626,213

Filing Date : July 24, 2003

Examiner : Schwadron

Title: METHODS AND COMPOSITIONS FOR IMMUNOTHERAPY OF B CELL
INVOLVEMENT IN PROMOTION OF A DISEASE CONDITION COMPRISING
MULTIPLE SCLEROSIS

Amendments to the Claims

1. (previously presented) A method for reducing a pro-multiple sclerosis immune response in an individual, wherein the pro-MS immune response comprises a humoral immune response induced against an epitope comprising terminal alpha 2,6 linked sialic acid on shed antigen, the method comprising administering to the individual a composition comprising an affinity ligand which selectively binds to a B cell determinant, wherein the B cell determinant is selected from the group consisting of CD19, CD20, CD21, CD22, Lym-1, and a determinant expressed only by B cells and not by immune cells other than B cells; wherein the B cells targeted by the method and by the composition are nonmalignant B cells, wherein the composition is administered in an amount effective to deplete B cells, and wherein the depletion of B cells results in reducing the pro-multiple sclerosis immune response induced against the epitope comprising terminal alpha 2,6 linked sialic acid.

2-17. (cancelled)

18. (previously presented) The method according to claim 1, wherein the nonmalignant B cells are B cells selected from the group consisting of mature B cells, memory B cells, CD19⁺sTn⁺ B cells, CD19⁺CD21⁺sTn⁺ B cells, and CD19⁺CD5⁺sTn⁺ B cells, and a combination thereof.

19. (withdrawn) The method according to claim 1, wherein the composition comprises a chimeric anti-CD20 monoclonal antibody.

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20. (previously presented) The method according to claim 1, wherein the composition is administered parenterally, or in a site directed method in which the composition is delivered into an access that directly supplies central nervous tissue undergoing demyelination.

21. (previously presented) The method according to claim 1, wherein the composition further comprises an additional component selected from the group consisting of one or more chemotherapeutic agents, an anti-inflammatory agent, a cytolytic agent, a pharmaceutically acceptable carrier, and a combination thereof.

22. (previously presented) The method according to claim 1, wherein the shed antigen comprises a glycolipid comprising one or more epitopes comprising terminal alpha 2,6 linked sialic acid.

23. (previously presented) The method according to claim 22, wherein glycolipid comprises a ganglioside.

24. (previously presented) The method according to claim 1, wherein the composition comprises an antibody.

25. (withdrawn) The method according to claim 1, wherein the composition is administered intravenously.

26. (previously presented) A site-directed method for reducing a pro-multiple sclerosis immune response in an individual, wherein the pro-multiple sclerosis immune response is a humoral immune response induced against an epitope comprising a terminal alpha 2,6 linked sialic acid

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on shed antigen, the method comprising administering to the individual a composition comprising an affinity ligand, which selectively binds to a B cell determinant, wherein the B cell determinant is selected from the group consisting of CD19, CD20, CD21, CD22, Lym-1, and a determinant expressed only by B cells and not by immune cells other than B cells; wherein B cells targeted by the method and by the composition are nonmalignant B cells, wherein the composition is delivered into an access that directly supplies central nervous tissue undergoing demyelination, wherein the composition is administered in an amount effective to deplete B cells, and wherein the depletion of B cells results in reducing the pro-multiple sclerosis immune response induced against the epitope comprising terminal alpha 2,6 linked sialic acid epitope.

27. (previously presented) The method according to claim 26, wherein the nonmalignant B cells are B cells selected from the group consisting of mature B cells, memory B cells, CD19⁺sTn⁺ B cells, CD19⁺CD21⁺sTn⁺ B cells, and CD19⁺CD5⁺sTn⁺ B cells, and a combination thereof.

28. (withdrawn) The method according to claim 26, wherein the composition comprises a chimeric anti-CD20 monoclonal antibody.

29. (previously presented) The method according to claim 26, wherein the composition further comprises an additional component selected from the group consisting of one or more chemotherapeutic agents, an anti-inflammatory agent, a cytolytic agent, a pharmaceutically acceptable carrier, and a combination thereof.

30. (previously presented) The method according to claim 26, wherein the shed antigen comprises a glycolipid comprising one or more epitopes comprising terminal alpha 2,6 linked sialic acid.

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31. (previously presented) The method according to claim 30, wherein glycolipid comprises a ganglioside.
32. (previously presented) The method according to claim 26, wherein the composition comprises an antibody.
33. (previously presented) A method for reducing a pro-multiple sclerosis immune response in an individual, wherein the pro-multiple sclerosis immune response is directed against an epitope comprising terminal alpha 2,6 linked sialic acid contained on shed antigen comprising a glycolipid, the method comprising administering to the individual a composition comprising a monoclonal antibody, wherein the monoclonal antibody binds to a B cell determinant selected from the group consisting of CD19, CD20, CD21, CD22, Lym-1, and a determinant expressed only by B cells and not by immune cells other than B cells; wherein B cells targeted by the method and by the composition are nonmalignant B cells, and wherein the composition is administered in an amount effective to deplete B cells such that said pro-MS immune response is reduced.
34. (previously presented) The method according to claim 33, wherein the nonmalignant B cells are B cells selected from the group consisting of mature B cells, memory B cells, CD19⁺sTn⁺ B cells, CD19⁺CD21⁺sTn⁺ B cells, and CD19⁺CD5⁺sTn⁺ B cells, and a combination thereof.
35. (withdrawn) The method according to claim 33, wherein the monoclonal antibody comprises a chimeric anti-CD20 monoclonal antibody.

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36. (previously presented) The method according to claim 33, wherein the composition further comprises an additional component selected from the group consisting of one or more chemotherapeutic agents, an anti-inflammatory agent, a cytolytic agent, a pharmaceutically acceptable carrier, and a combination thereof.

37. (previously presented) The method according to claim 33, wherein glycolipid comprises a ganglioside.

38. (previously presented) A method for treating inflammation associated with multiple sclerosis, wherein the inflammation is caused by a humoral immune response against a shed antigen comprising an epitope comprising a terminal alpha 2,6 linked sialic acid, the method comprising depleting B cells to inhibit said humoral immune response by administering an amount of a composition effective to deplete B cells and reduce said humoral immune response against the shed antigen, wherein the composition comprises an affinity ligand which binds to a B cell determinant selected from the group consisting of CD19, CD20, CD21, CD22, Lym-1, and a determinant expressed only by the B cells and not by immune cells other than B cells; and wherein B cells targeted by the method and by the composition are nonmalignant B cells.

39. (previously presented) The method according to claim 38, wherein the nonmalignant B cells are B cells selected from the group consisting of mature B cells, memory B cells, CD19⁺sTn⁺ B cells, CD19⁺CD21⁺sTn⁺ B cells, and CD19⁺CD5⁺sTn⁺ B cells, or a combination thereof.

40. (withdrawn) The method according to claim 38, wherein the composition comprises a chimeric anti-CD20 monoclonal antibody.

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41. (previously presented) The method according to claim 38, wherein the composition further comprises an additional component selected from the group consisting of one or more chemotherapeutic agents, an anti-inflammatory agent, a cytolytic agent, a pharmaceutically acceptable carrier, and a combination thereof.
42. (previously presented) The method according to claim 38, wherein the composition comprises a monoclonal antibody.
43. (previously presented) The method according to claim 38, wherein the shed antigen comprises a glycolipid comprising one or more epitopes comprising terminal alpha 2,6 linked sialic acid.
44. (previously presented) The method according to claim 43, wherein glycolipid comprises a ganglioside.
45. (Currently amended) A method for reducing a pro-multiple sclerosis immune response comprising administering to an individual an affinity ligand which selectively binds to a B cell determinant of a shed antigen-specific B cell, wherein the B cells are nonmalignant B cells, and wherein the affinity ligand is administered in an amount effective to deplete B cells.
46. (previously presented) The method according to claim 45, wherein the B cell determinant is selected from the group consisting of CD19, CD20, CD21, CD22 Lym-1 and a determinant expressed only by the B cells and not by immune cells other than B cells.

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47. (previously presented) The method according to claim 45, wherein the nonmalignant B cells are B cells selected from the group consisting of mature B cells, memory B cells, CD19⁺sTn⁺ B cells, CD19⁺CD21⁺sTn⁺ B cells, and CD19⁺CD5⁺sTn⁺ B cells, or a combination thereof.

48. (previously presented) The method according to claim 45, wherein the shed antigen-specific B cells have specificity for an epitope comprising terminal alpha 2, 6 linked sialic acid.